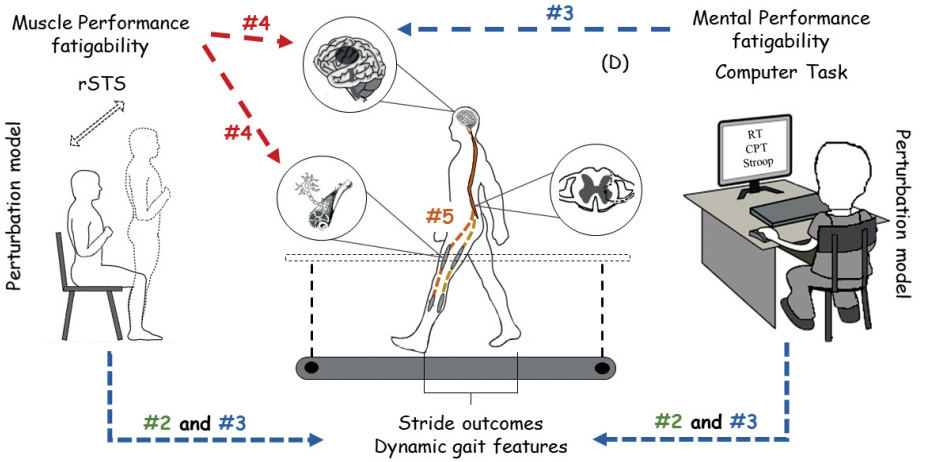
General Discussion

This thesis examined the effects of age on gait adaptability following experimentally induced fatigue. Figure 1 illustrates the experimental design and summarizes the main findings by chapter. In chapter 2, the systematic review revealed that although fatigability affects spatial and temporal features of gait according to the type of fatigue, the underlying mechanism of muscle and mental fatigability remains unclear. In chapter 3, we found that muscle and mental fatigability minimally affected healthy young and older adults' gait, possibly because treadmill walking made gait uniform. We interpret the data to mean that: 1) mental fatigability might elicit effects whenever walking is coupled with higher cognitive involvement (e.g., dual-task walking); 2) age-dependent neuromuscular modulation might compensate for the fatigability effects to maintain gait performance; and/or 3) the repetitive sit-to-stand task might not specifically induce substantial changes in key elements of gait, thereby limiting the scope of this protocol to examine age-related gait adaptations to fatigue. In chapter 4, we examined the effects of age and exhaustive repetitive sit-to-stand on muscle activation during ascent and descent phases of the sit-to-stand task. We found that by performing remarkably fewer sit-to-stand trials, older adults had minimized fatigability effects on muscle activation, voluntary force, and motor function, producing minimal changes in stride outcomes and gait dynamics after repetitive sit-to-stand seen in Chapter 3. However, Chapter 5 shows that notwithstanding the subtle modifications in muscle activation and voluntary force, repetitive sit-to-stand produced an age-specific compensatory strategy in the neural drive to maintain gait performance.



Chapter #2

OA - Muscle fatigability affected stride outcomes and variability, more during overground vs. treadmill walking

OA – Mental fatigability increased the stride outcomes variability (6-16%) in dual-task only

Chapter #3

OA and YA - Minimal effects of rSTS and computer task on stride of treadmill walking

Treadmill may have limited the fatigability effects on gait

Chapter #4

OA vs. YA performed 467 fewer STS trials

OA and YA - rSTS decreased subtle (16-28%) the level force and muscle activation

OA vs. YA performed less STS trials, potentially avoiding greater fatigue effects in muscle force and activation.

The scope of rSTS is limited to probe the age-effects on muscle adaptation in gait and posture

Chapter #5

OA vs. YA had 43% to 62% lower coherence between GL-SL, RF-VL and TA-PL during treadmill walking

OA and YA increased 16% the TA-PL coherence during gait after rSTS

OA vs. YA increased by 23% the GL-SL after rSTS

rSTS elicits an age-specific compensatory strategy in the neural drive to maintain gait performance

Figure 1. Schematic representation of the experimental set-up with a summary of the main finding in each chapter. OA=Older adults; YA = Younger adults; STS=Sit-to-stand; rSTS= repetitive STS; TA=Tibialis anterior; PL=Peroneus longus; GL=Gastrocnemius lateralis; SL=Soleus; RF=Rectus femoris; VL=Vastus lateralis

1. FATIGUE AND AGE EFFECTS ON STRIDE OUTCOMES AND DYNAMIC FEATURES OF GAIT

After experimentally induced fatiguability, the most often observed changes occurred in stride outcomes and gait dynamics (Chapter 2, Table 2 [1–7]), both becoming more pronounced for induced fatigue-type specificity (specific vs. non-specific gait fatigability protocols) and for gait assessment (overground vs. treadmill walking) (Chapter 2, [1,3,4]).

From the perspective of fatigue-type specificity, although fatigability evokes adaptations in spatial and temporal stride outcomes and dynamics gait features, those adaptations were moderate or even subtle depending on how specific the fatigability protocol and the gait conditions were [1]. Local specific muscle fatigability evokes only small adjustments of stride outcomes during treadmill walking (e.g., 2cm (2%) of decreased stride length (Chapter 3 [8])) and overground walking (e.g., 4 to 5 cm (3-5%) of increased stride length [6,7]), even in a protocol that targeted a decrease of 50% in the relative maximum knee torque [7]. Such small results indicated that non-specific gait fatigability, such as repetitive sit-to-stand and dynamometer exercise, might not be optimal to perturb the gait necessitating substantial adaptations.

Presumably, non-specific gait fatigability protocols do not target specific key elements of gait, such as those pertaining to rhythm/temporal activation control (central pattern generators) and the magnitude of muscle activation driven by cortical inputs [9]. Thus, gait would not be perturbed because the key elements of gait control can operate within a normal range. This hypothesis is partially supported by the literature that indicates substantial changes in stride outcomes after fatigability induced by specific gait protocol (e.g.,18% increase in stride velocity after fatiguability induced by incremental walking task) [5]. On the other hand, despite some substantial gait adaption to specific gait fatigability protocols [2], the gait adaptability to fatigability remains inconclusive in healthy older adults [10,11]. For example, long-distance walking for 30 min increased asymmetry on ankle and knee angular velocity variabilities, but inexplicably, those increases were mitigated after 60 min of treadmill walking [11].

Concerning mental performance fatigability, interference with cognitive resources due to fatigability indicated to be a useful model to perturb gait in dual-task overground walking [1,12]. This concept is indeed supported by previous evidence that suggested that mental-fatigability affected gait variability (e.g., increase by 4 to 16% in coefficients of variations in stride metrics) during dual- but not single-

task in older adults' overground walking [12]. Therefore, age-related adaptability to mental performance fatigability is likely apparent only during walking conditions with high cognitive involvement. Such apparent effects of mental fatigue on gait performance during dual-task walking in older adults might be evident because, when gait control is perturbed, older adults prioritize gait adaptation at the expense of cognitive performance [13].

Fatigability effects on gait appear to be influenced by conditions in which gait is assessed. More overt effect of experimentally induced fatigability was observed during gait protocol in overground vs. treadmill walking situation. Presumably, the invariant pattern imposed by the treadmill [14,15] minimizes any potential age-related adaptation to experimentally induced fatigability. In contrast, walking situations that simulate real-life walking (e.g., overground walking), or even more complex condition (e.g., combine fatigue with external walking perturbation, obstacle avoidance, stair gait) require more active gait control and may represent higher susceptibility to the fatigability effects compared to treadmill walking [14,16].

While numerous studies focused on age-associated adaptability in stride outcomes in response to performance and perceived fatigability (Chapter 2, [1–3,5,7,17–20]), the underlying neural mechanism of gait adaptability due to fatigability remain mostly unanswered. Curiously, these studies indirectly attributed changes in stride outcomes to the effects of induced fatigability on neuromuscular control [2,3,5,7,17–20], but failed in analyzing it. Specifically considering the present data, we suggest that age-dependent modulations in the common neural drive (intermuscular coherence) might have compensated for the muscle performance fatigability effects on gait. Thus, the participants could keep the stride metrics of gait performance unchanged after repetitive sit-to-stand.

In chapter 5, we examined if age-dependent modulation in neuromuscular control may be mediating the fatigability effects on gait metrics. The first new observation was that age-related reduction (45 to 68%) in beta-band coherence extended the previous findings [21–23] to be present not only in ankle dorsiflexor (Tibialis anterior and Peroneus longus) but also in gastrocnemius lateralis-Soleus and Rectus femoris-Vastus Lateralis muscle pairs. Reduced beta-band coherence, indicative of corticomuscular communication, in older adults might be indicative of inefficiency in the central nervous system to reduce the dimensionality by sending common drives to muscles that exert similar functions [24]. This assumption is plausible because it is widely assumed that intermuscular beta-band coherence may happen from pooled inputs via branched corticospinal tracts [24–27]. This inefficiency in the central nervous system in

reducing the dimensionally motor control would impair the synchronization of muscle units firing [28], affecting motor coordination. It explains the poor gait performance in older adults (Chapter 3 and Chapter 5) and would signalize higher energy cost to control coordinated movement, as gait [29]. Age-specific modulation in coherence before repetitive sit-to-stand point to the necessity of further compensatory neural modulation due to fatigability, mainly in the old group.

Indeed, our data indicated an age-specific modulation in neuromuscular control during gait after fatigability (Chapter 5). Such age-modulation was mostly observed by a specific increase (~23 to 49 %) in Gastrocnemius Lateralis-Soleus coherence in swing and Tibialis Anterior-Peroneus Longus in stance phases in older adults. While in younger, a decrease in Gastrocnemius Lateralis-Soleus coherence (~23%) and only a slight increase in the Tibialis Anterior-Peroneus Longus (1%) was witnessed. This modulation suggests that older adults evoked compensatory neural strategy to compensate muscle fatigability, indicated by a strengthening in common neural inputs via branched corticospinal tracts. Strengthened coherence is described as a compensatory attempt of the central nervous system in reducing the dimensionality of the motor system to send shared drives to two close synergistic muscles during gait [9,30]. Presumably, age-specific neuromuscular gait modulation due to muscle fatigability might occur because of age-specific neuromuscular deterioration. Such neuromuscular deterioration contributes to age-related changes in mechanical output during gait [31], causing older adults to evoke a compensatory neural strategy due to muscle fatigability to keep the stride metrics of treadmill walking unchanged (Chapter 3 and Chapter 5).

2. FATIGUE AS A MODEL TO UNDERSTAND AGE-RELATED GAIT ADAPTABILITY

Experimentally induced fatigability as a perturbation model has been extensively used to examine age-related adaptability in functional tasks (e.g., postural and gait [12,32,33]). Those studies explained alterations in behavioral outcomes of a subsequent gait and posture through the physiologic and psychological effects of the perturbation model. However, these protocols failed in measuring the perturbation model per se, which unsubstantiated all the explanation for the age-related adaptability to fatigability. In chapter 4, we verified the age-specific changes in muscle activation due to repetitive sit-to-stand, muscle fatigability model. Additionally, although we did not test, we also explored the literature to understand how demanding mental tasks would impair movement control.

2.1. Repetitive sit-to-stand as a perturbation model

While numerous studies used repetitive sit-to-stand as a perturbation model to examine age-related adaptability in gait [4,6,8,19,34], the reason for the use of the repetitive sit-to-stand as fatigability perturbation is unclear. Our suspicion for this widespread usage of repetitive sit-to-stand is because sit-to-stand is one of the most muscle demanding functional tasks [35–37], which requires relatively higher muscle effort compared even with ascent or descent of stairs [1]. In addition, repetitive sit-to-stand is particularly harder for older vs. younger adults to execute due to the age-typical degenerative process in neuromuscular function [38].

In chapter 4, we determined the effects of repetitive sit-to-stand on muscle activation during initial- and late-stages of sit-to-stand and on maximum force to probe the repetitive sit-to-stand as a perturbation model to examine age-related gait adaptability. The most notable evidence was an overwhelmingly increasing in rate of perceived exertion that accompanied 467 fewer sit-to-stand trials in older (134) vs. younger adults (601). While older and younger adults signalized to be unable to continue with sit-to-stand, the reduction in the maximum voluntary isometric force and knee and dorsiflexor activation, in both age groups, were limited to 16% and 25%, respectively. The relatively subtle decrease in the level of maximal force and electromyography activation after hundreds of sit-to-stand trials point to the potential limitation of this task as a perturbation model to explore age-effects on gait adaptability.

Combining repetitive sit-to-stand performance, and its effects on muscle force and activation, it seems plausible that older adults, to perform a drastically reduced number of sit-to-stand trials, had spared knee extensors from becoming dysfunctional. This observation is endorsed by other studies that verified even small effects of repetitive sit-to-stand on the maximal torque (7 to 10%) [18,19]. Such sparing effects of repetitive sit-to-stand on muscle function may underlie the trivial changes in gait biomechanics in obstacle crossing tasks [19] and minimal effects of repetitive sit-to-stand on treadmill walking performance (Chapter 2 and 3 [1,8]).

Curiously, even with limited effects, repetitive sit-to-stand elicits an age-specific compensatory strategy in the neural drive to maintain unchanged gait performance. The age-specific modulations in the neural drive during treadmill walking were accompanied by the repetitive sit-to-stand effects on muscle force and activation. However, it is perhaps pretentious to assume that age-specific modulation in Tibial anterior-Peroneus Longus, Gastrocnemius Lateralis-Soleus and Rectus Femoris-Vastus Lateralis is entirely consequences of repetitive sit-to-stand since changes

between repetitive sit-to-stand outcomes and coherence did not correlate (r=0.20 to 0.38; p>0.05, Chapter 5). Instead, it seems reasonable that the age-specific modulation in common neural drive during treadmill walking after repetitive sit-to-stand may arise from a combination of subtle changes in muscle activation, maximum torque [39,40], the overwhelming increase in rate of perceived exertion due to fatigability (signal of central fatigue) [41], age-related degeneration in neuromuscular control [21,23], and possible changes in somatosensorial feedback due to repetitive sit-to-stand (not assessed here) that impair the neural control of gait [9]. Altogether, the arguments indicate a limitation of repetitive sit-to-stand as a perturbation model to examine age-related gait adaptabilities.

2.2. Demanding mental task as a perturbation model

Mental performance fatigability is described as a psychophysiological state due to prolonged exposure to a demanding mental task [42,43]. While psychologically this state is associated to a decline in motivation accompanied by increased self-reported fillings of tiredness [44], physiologically mental performance fatigability is, for example, related to changes in brain activity across Alpha, Beta and Theta bands in frontal, central and posterior brain areas [45]. Together, it is reasonable to believe that mental performance would affect the top-down control of movement [46], but, mainly, in a task in which the allocation of cognitive resources/functions is highly required [12]. In this sense, experimental protocol as a single task treadmill walking or standing postural task in which the cognitive involvement is small, the effects of mental performance fatigability may be minimal or even absent [8,33]. Conceivably, demanding mental tasks would be an appropriate model to examine age-related adaptation to mental fatigability in dual-task walking task [12], preferably in more active gait conditions, such as overground walking.

3. LIMITATION AND FUTURE DIRECTIONS

Collectively the results suggest that protocols of induced fatigability may evoke adaptations in a fatigability-type specific way. For this reason, high muscle demanding fatigability protocols that target specific key elements of gait might be useful to examine the effects of age and fatigue on gait adaptability [10]. In addition, there is a need to determine the effects of muscle performance fatigability on motor outcomes that are both specific and not specific to the fatiguing task, an approach that would improve experimental control and the validity of conclusions. Further studies should drive the hypothesis not only for the

strides outcomes but focus on understanding the underlying neural mechanism related to muscle fatigability effects in older adults' gait mechanics.

Using a treadmill to examine the effects of age and fatigue in gait adaptability can minimize such effects because treadmill walking minimizes gait variability [14,47]. Possibly, this treadmill influence may have mitigated the mental and muscle fatigability effects on gait. Thus, assessing gait adaptability to experimentally induced fatigability during more reactive gait control, such as overground walking, or even more complex gait conditions (e.g., perturbed gait, obstacle crossing, dual-task walking, step up and down in a curb) can augment the potential effects of fatigability in gait [1]. Since age-related changes in gait are pronounced in these gait conditions [48–50], such complex gait would also increase the niche for examining the age and fatigability effects on gait.

Especially regarding mental performance fatigability, although demanding mental tasks effectively induced mental performance fatigability (Chapter 3), the adaptability on gait evoked by this protocol was minimal. Probably, healthy subjects would walk without any effect of mental fatigability because small cognitive resources are required during single treadmill walking. Future studies that intend to understand the effects of mental performance fatigability during gait should consider examining dual-task walking. We also suspect that if such fatiguing protocols focus on a specific cognitive function, e.g., attention, the secondary task during dual-task walking should also have high involvement of the specific cognitive function (attention). These specifics aspects of the task are likely determinant to examine mental fatigability effects on gait adaptability.

Limitations of this thesis also involve the characteristics of the participants. The two age groups were functionally similar (as observed by physical performance tasks, global cognition, and trait of fatigue), representing an unusually healthy segment of older adults. However, the similarity between the two age groups eliminated "confounders" functional differences, permitting us to examine a "purer" age-effect. Studies with fatigability protocols applied for a "typical" segment of older adults would broaden the scope and can be more representative of this population. It would also magnify the age-specific modulation for fatigue. Still considering population selection, perhaps, the most critical gap in knowledge is related to comparative studies of gait adaptation in older adults with and without self-reported fatigue. Such studies would provide meaningful insights into adaptations in healthy older adults after experimentally induced muscle or mental fatigability.

4. CONCLUSIONS

This thesis examined the effect of age and experimentally induced mental and muscle fatigability on gait. Muscle and mental fatigability had minimal effects on stride outcomes and dynamic gait features in younger and healthy older adults, possibly because treadmill walking makes gait uniform. We surmised that the overwhelming increase in perceived fatigue produced by repetitive sit-to-stand in older adults was accompanied by only subtle modifications in muscle force and activation, limiting the scope of this perturbation model to probe the age-effects on muscle adaptation in gait and posture. The effects of age and fatigability might be more overt during real-life or complex walking tasks (dual-task, perturbed walking) compared with treadmill walking and, perhaps, more effective model for examining gait and age adaptability to fatigability should considering specific gait fatigue-type. However, even with limited effects, repetitive sit-to-stand elicits age-specific changes in the neural drive, which could be interpreted as compensation for fatigue to maintain gait performance.

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